UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,357	06/12/2008	Olivera Josimovic-Alasevic	101215-230	7604

27387 7590 04/11/2011

LONDA, BRUCE S.
NORRIS MCLAUGHLIN & MARCUS, PA
875 THIRD AVE, 8TH FLOOR
NEW YORK, NY 10022

EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	
MAIL DATE	DELIVERY MODE
04/11/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,357	JOSIMOVIC-ALASEVIC ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-16* is/are pending in the application.

4a) Of the above claim(s) *7-12,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 2-6, 13 and 14) in the reply filed on 3/18/2011 is acknowledged.

Claims 7-12, 15, and 16 are withdrawn from consideration as being drawn to non-elected subject matter. Claims 2-6, 13 and 14 have been considered on the merits.

Drawings

The drawings are objected to because the images are invisible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the producing intervertebral disk cells having capacity of proliferation and differentiation only autologous or allogenic culturing and culturing with no antibiotic and fungistatic agents, does not reasonably provide enablement for those culture condition including antibiotics and/or fungicides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims disclose a method of producing intervertebral disk cell transplants or intervertebral disk tissue transplants by isolating intervertebral disk cells from degenerate prolapsed intervertebral disk tissue and culturing as monolayer in the presence of autologous serum, and such culturing condition would necessarily form intervertebral disk cell transplants having the capability of proliferation, migration and differentiation.

According to the specification, however, there appears to be additional critical feature required for obtaining the intervertebral disk cell transplants having the capability of proliferation, migration and differentiation. The specification clearly discloses that such requirement is specifically directed to the addition autologous serum only, without addition of exogenic growth-promoting compounds and without addition of antibiotics

(p.8). Similarly, it is disclosed that only autologous or allogenic culturing of the cells and cell aggregates and culturing with no antibiotic and fungistatic agents allows non-affected proliferation and differentiation of the cells in the monolayer culture and undisturbed formation of the specific matrix within the cell aggregates (p.12, 2nd par.). Therefore, the broad limitation directed to the culture condition in the instant claims would not be sufficient to form the claimed cell population having capability of proliferation, migration and differentiation. Applicant is advised to amend the limitation directed to the culture condition accordingly to overcome the instant claim rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-6, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-4 disclose the wherein clause directed to the ratio of alpha-MEM medium and HAM-F12 medium. It is not clear whether these mixed medium is directed to the term "a cell culture medium", or these media are different from the cell culture medium for intervertebral disk tissue culture, and if different, it is vague what the purpose of the mixed media of the clause would be. Clarification is required.

The phrase "having a humidity of 85-95%" in claims 2 and 3 does not clearly point out what subject matter would have the humidity of the claimed range. Clarification is required.

The term "autologous" in claims 2-6, 13 and 14 does not clearly point out whether the serum is autologous to the cells (intervertebral disk cells) or it is autologous to the recipient of the cell or tissue transplants of the claimed invention. Since the claims do not clearly disclose whether the intervertebral disk cells are autologous, they can be heterologous or allogeneic to the recipient of the cell/tissue transplants. If so, it is not clear whether "autologous serum" of the claimed invention could be autologous to the cells or the recipient of the transplants. Clarification is required.

The term "internal" in claim 13, line 5 is not clear what subject matter the term intends to point out. What are "internal vital, differentiated cells"?

Claims 3 and 13 discloses that the intervertebral disk cell transplants can form matrix structure or 3D intervertebral disk tissue transplants by culturing with addition of autologous serum. It is not clear whether the mere addition of autologous serum would necessarily form intervertebral disk tissue transplants from the intervertebral disk cell transplants. It appears that the further detailed culture condition is critical and required for the claimed invention. Since the culture condition (i.e. addition of autologous serum) is identical to the steps of forming the intervertebral disk cell transplants as disclosed in claims 2 and 6, it is not clear how the intervertebral disk cell transplants can form 3D intervertebral disk tissue transplants. Applicant is advised to incorporate the limitation of claim 5 into claim 13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-6, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Masuda et al. (US 2003/0229400) in view of Okuma et al. (2000, J. Ortho. Res.; IDS ref.) and Masuda et al. (US 2003/0165473; of record) in further view of Libera et al. (WO/2001/68811; for English translation US 2003/0153078 is relied on).

Masuda et al. teach a method of culturing intervertebral disc cells in the presence of autologous serum and in monolayer (par. 10, 27, 34, 42, 66).

It is well known in the art that intervertebral disc is composed of nucleus pulposus and annulus fibrosus, and Masuda et al. also teach chondrogenic cells can be obtained from either nucleus pulposus or annulus fibrosus (par. 34).

Furthermore, with regard to the limitation of claim 14 directed to the mixture of annulus fibrosus and nucleus pulposus cells, since either nucleus pulposus or annulus fibrosus cells can be used for chondrogenic cells, it would have been obvious to use mixed chondrogenic cells derived from each nucleus pulposus and annulus fibrosus.

M.P.E.P. §2144.06 states "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious).

Masuda et al. ('400) do not teach that the intervertebral disc cells are isolated from degenerate prolapsed or affected intervertebral disk tissue.

Okuma et al. teach a method of reinserting autogenous (autologous) nucleus pulposus cells isolated from degenerate intervertebral disc (lumbar disc).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to utilize autologous intervertebral disc cells from the patient or subject having degenerate intervertebral disc in the method of Masuda et al. since one skilled in the art would recognize that autologous nucleus pulposus cells can be utilized for intervertebral disc cell transplant source based on the teaching of Okuma et

al., and thus motivated to try autologous intervertebral disc cells from the damaged or degenerate intervertebral disc.

Regarding the culture condition directed to the medium type, the amount of autologous serum, the temperature, the CO_2 content and the humidity for the claimed method, it is considered that these limitations are well known parameters to be optimized by routine experimentations. Furthermore it is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in In re Aller, Lacey, and Haft, 105 USPQ 233 (CCPA 1955): Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931,24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are

disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11,57 USPQ 136. (Emphasis added). With regards to determining experimental parameters, such as time in culture, the court has held that "[d]iscovery of optimum value of result effective variable in known process is ordinarily within skill of art (In re Boesch and Slaney, 205 USPQ 215 (CCPA 1980)).

Regarding the step of culturing the intervertebral disc cells under the three-dimensional culture conditions forming intervertebral disc tissue transplants, Masuda et al. (‘473) teach a method of culturing implantable intervertebral disc tissue as suspension culture to form cell aggregates, and thus, one skilled in the art would recognize that the intervertebral disc cells of Masuda et al. (‘400) can be formed 3D aggregates for transplantation as taught by Masuda et al. (‘473), And it would have been obvious to a person of ordinary skill in the art to try the steps of culturing intervertebral disc cells of Masuda et al. (‘400) in suspension to from 3D aggregates of intervertebral disc tissue transplants.

With regard to the limitation to the culture vessel having hydrophobic surface and tapering bottom, it is well known in the art that the suspension culture for 3D aggregates utilizes the culture plate having the hydrophobic surface and a tapered bottom according to Libera et al. (par. 8, 18). It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to try to use the cell culture

vessel of Libera et al. for the method of Masuda et al. ('400) in view of Masuda et al. ('473) with a reasonable expectation of success.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651